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AMENDMENTS

Please amend the claim set to read as follows.

1.   (currently amended) A method for obtaining an siRNA molecule for a target gene, wherein said siRNA molecule comprises an antisense region that is 19 – 25 nucleotide bases in length and a sense region that is 19 – 25 nucleotide bases in length, wherein said sense region and said antisense region form a duplex region of 19-25 nucleotide base pairs, said method comprising the steps:

(a) selecting a target gene;

(b) identifying a set of candidate siRNA sequences, wherein the antisense region of each of said candidate siRNA sequences is at least 79% complementary to a region of the target gene;

(c) applying **a computer algorithm to each of said candidate siRNA sequences, wherein said computer algorithm comprises** a criterion ~~to each of said candidate siRNA sequences, wherein the criterion is~~ selected from the group consisting of: (i) within said duplex region the number of A and U nucleotides present in the first five nucleotide positions at the 5' terminus of the antisense region is higher than that present in the last five nucleotide positions at the 3' terminus of the antisense region; (ii) within said duplex region the number of A and U nucleotides present in the first four positions at the 5' terminus of the antisense region is higher than that present in the last four positions at the 3' terminus of the antisense region; (iii) within said duplex region the number of A and U nucleotides present in the first three positions at the 5' terminus of the antisense region is higher than that present in the last three positions at the 3' terminus of the antisense region; (iv) within said duplex region the number of A and U nucleotides present in the first two positions at the 5' terminus of the antisense region is higher than that present in the last two positions at the 3' terminus of the antisense region; and (v) within said duplex region the first 5' position of the antisense region has either an A or U nucleotide and the last 3' position of the antisense region has neither an A nor U nucleotide;

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(d) **after step (c)** selecting a candidate siRNA sequence from the set of candidate siRNA sequences of step (b) as an siRNA sequence for the target gene, if said candidate siRNA sequence satisfies said criterion; and

(e) **after step (d)** synthesizing an siRNA molecule for said target gene, wherein said siRNA molecule for said target gene comprises said siRNA sequence for the target gene, whereby said siRNA molecule for said target gene is obtained.

2. (canceled)

3. (canceled)

4. (canceled)

5. (canceled)

6. (canceled)

7. (canceled)

8. (canceled)

9. (canceled)

10. (canceled)

11. (canceled)

12. (canceled)

13. (canceled)

14. (canceled)

15. (canceled)

16. (canceled)

17. (canceled)

18. (canceled)

19. (canceled)

20. (canceled)

21. (canceled)

22. (canceled)

23. (canceled)

24. (canceled)

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25. (canceled)

26. (canceled)

27. (canceled)

28. (canceled)

29. (canceled)

30. (canceled)

31. (canceled)

32. (canceled)

33. (canceled)

34. (canceled)

35. (canceled)

36. (canceled)

37. (canceled)

38. (previously presented) The method according to claim 1, wherein the criterion is: within said duplex region the number of A and U nucleotides present in the first five nucleotide positions at the 5' terminus of the antisense region is higher than that present in the last five nucleotide positions at the 3' terminus of the antisense region.

39. (previously presented) The method according to claim 1, wherein the criterion is: within said duplex region the number of A and U nucleotides present in the first four positions at the 5' terminus of the antisense region is higher than that present in the last four positions at the 3' terminus of the antisense region.

40. (previously presented) The method according to claim 1, wherein the criterion is: within said duplex region the number of A and U nucleotides present in the first three positions at the 5' terminus of the antisense region is higher than that present in the last three positions at the 3' terminus of the antisense region.

41. (previously presented) The method according to claim 1, wherein the criterion is: within said duplex region the number of A and U nucleotides present in the first two

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positions at the 5' terminus of the antisense region is higher than that present in the last two positions at the 3' terminus of the antisense region.

42. (previously presented) The method according to claim 1, wherein the criterion is: within said duplex region the first 5' position of the antisense region has either an A or U nucleotide and the last 3' position of the antisense region had neither an A nor U nucleotide.

43. (currently amended) A method for obtaining an siRNA molecule for a target gene, wherein said siRNA molecule comprises an antisense sequence that is 19 – 30 nucleotide bases in length and a sense sequence that is 19 – 30 nucleotide bases in length and said antisense sequence and said sense sequence form a duplex region of 19-30 base pairs, said method comprising the steps:

   (a) selecting a target gene;

   (b) identifying a set of candidate siRNA sequences, wherein the antisense sequence of each of said candidate siRNA sequences is at least 79% complementary to a region of the target gene;

   (c) applying to each of said candidate siRNA sequences **a computer algorithm, wherein said computer algorithm comprises** a set of one or more criteria selected from the group consisting of a presence of U at position 1 of the antisense sequence, a presence of U at position 17 of the antisense sequence, a presence of A at position 10 of the antisense sequence, a presence of U at position 6 of the antisense sequence, an absence of G at position 1 of the antisense sequence, an absence of C at position 7 of the antisense sequence, an absence of A at position 15 of the antisense sequence and an absence of U at position 9 of the antisense sequence, wherein said positions are defined in reference to the 5' end of the antisense sequence ~~within said duplex region~~;

   (d) **after step (c)** selecting a candidate siRNA sequence from the set of candidate siRNA sequences of step (b) as an siRNA sequence for the target gene, if said candidate siRNA sequence satisfies said set of one or more criteria; and

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(e) **after step (d)** synthesizing an siRNA molecule for said target gene, wherein said siRNA molecule for said target gene comprises said siRNA sequence for the target gene, whereby said siRNA molecule for said target gene is obtained.

44. (previously presented) The method according to claim 43, wherein the set of one or more criteria includes the presence of U at position 1 of the antisense sequence.

45. (previously presented) The method according to claim 43, wherein the set of one or more criteria includes the presence of U at position 17 of the antisense sequence.

46. (previously presented) The method according to claim 43, wherein the set of one or more criteria includes the presence of A at position 10 of the antisense sequence.

47. (previously presented) The method according to claim 43, wherein the set of one or more criteria includes the presence of U at position 6 of the antisense sequence.

48. (previously presented) The method according to claim 43, wherein the set of one or more criteria includes the absence of G at position 1 of the antisense sequence.

49. (previously presented) The method according to claim 43, wherein the set of one or more criteria includes the absence of C at position 7 of the antisense sequence.

50. (previously presented) The method according to claim 43, wherein the set of one or more criteria includes the absence of A at position 15 of the antisense sequence.

51. (previously presented) The method according to claim 43, wherein the set of one or more criteria includes the absence of U at position 9 of the antisense sequence.

52. (previously presented) The method according to claim 43 further comprising applying one or more additional criteria selected from the group consisting of: a GC content between about 30% and 52%, and at least 2 A or U bases at positions 1 –5 of the

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antisense sequence, and selecting said candidate siRNA sequence if said candidate siRNA sequence satisfies said one or more additional criteria.

53. (previously presented) The method according to claim 43, wherein said candidate siRNA sequence is selected as said siRNA sequence for the target gene if said candidate siRNA sequence satisfies at least two criteria selected from the group consisting of: the presence of U at position 1 of the antisense sequence, the presence of U at position 17 of the antisense sequence, the presence of A at position 10 of the antisense sequence, the presence of U at position 6 of the antisense sequence, the absence of G at position 1 of the antisense sequence, the absence of C at position 7 of the antisense sequence, the absence of A at position 15 of the antisense sequence, and the absence of U at position 9 of the antisense sequence.

54. (previously presented) The method according to claim 43, wherein said candidate siRNA sequence is selected as said siRNA sequence for the target gene if said candidate siRNA sequence satisfies at least three criteria selected from the group consisting of: the presence of U at position 1 of the antisense sequence, the presence of U at position 17 of the antisense sequence, the presence of A at position 10 of the antisense sequence, the presence of U at position 6 of the antisense sequence, the absence of G at position 1 of the antisense sequence, the absence of C at position 7 of the antisense sequence, the absence of A at position 15 of the antisense sequence, and the absence of U at position 9 of the antisense sequence.

55. (canceled)

56. (canceled)

57. (previously presented) The method according to claim 43, wherein in (c) said method comprises applying the following criteria to each of said candidate siRNA sequences, the presence of U at position 1 of the antisense sequence, the presence of U at position 17 of the antisense sequence, the absence of G at position 1 of the antisense

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sequence, the absence of C at position 7 of the antisense sequence, and further comprises applying each of the following additional criteria to each of the candidate siRNA sequences: a GC content between about 30% and 52%, and at least 2 A or U bases at position 1 –5 of the antisense sequence, and in (d) selecting said candidate siRNA sequence as said siRNA sequence for said target gene if said candidate siRNA sequence satisfies the criteria of the presence of U at position 1 of the antisense sequence, the presence of U at position 17 of the antisense sequence, the absence of G at position 1 of the antisense sequence, the absence of C at position 7 of the antisense sequence, the GC content between about 30% and 52%, and at least 2 A or U bases at position 1 – 5 of the antisense sequence.

58. (previously presented) The method according to claim 43, wherein in (c) said method comprises applying the criteria of the absence of C at position 7 of the antisense sequence and further comprises applying the criteria of a GC content of between 30% and 52% and in (d) selecting said candidate siRNA sequence as said siRNA sequence for said target gene if said siRNA sequence satisfies both of said criteria of the absence of C at position 7 of the antisense sequence and the GC content of between 30% and 52%.

59. (previously presented) The method according to claim 43, wherein said candidate siRNA sequence is selected as said siRNA sequence for the target gene if said candidate siRNA sequence satisfies each of the following criteria: the absence of G at position 1 of the antisense sequence and the absence of C at position 7 of the antisense sequence.

60. (previously presented) The method according to claim 43, wherein in (c), said method comprises applying the criteria of the absence of C at position 7 and further comprises applying the criteria of: a GC content of between 30% and 52%, and wherein in (d) said method comprises selecting said candidate siRNA sequence as said siRNA sequence for said target gene if said siRNA sequence satisfies all of the

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criteria of the absence of C at position 7 of the antisense sequence, and the GC content of between 30% and 52%.

61. (currently amended) A method for selecting an siRNA sequence for a target gene, wherein said siRNA sequence comprises an antisense region that is 19 – 25 nucleotide bases in length and a sense region that is 19 – 25 nucleotide bases in length and said antisense sequence and said sense sequence form a duplex region of 19-25 base pairs, said method comprising the steps:

(a)   selecting a target gene;

(b)   identifying a set of candidate siRNA sequences, wherein the antisense region of each of said candidate siRNA sequences is at least 79% complementary to a region of the target gene;

(c)   applying **a computer algorithm to each of said candidate siRNA sequences, wherein said computer algorithm comprises** a criterion ~~to each of said candidate siRNA sequences, wherein the criterion is~~ selected from the group consisting of: (i) within said duplex region the number of A and U nucleotides present in the first five nucleotide positions at the 5' terminus of the antisense region is higher than that present in the last five nucleotide positions at the 3' terminus of the antisense region; (ii) within said duplex region the number of A and U nucleotides present in the first four positions at the 5' terminus of the antisense region is higher than that present in the last four positions at the 3' terminus of the antisense region; (iii) within said duplex region the number of A and U nucleotides present in the first three positions at the 5' terminus of the antisense region is higher than that present in the last three positions at the 3' terminus of the antisense region; (iv) within said duplex region the number of A and U nucleotides present in the first two positions at the 5' terminus of the antisense region is higher than that present in the last two positions at the 3' terminus of the antisense region; and (v) within said duplex region the first 5' position of the antisense region has either an A or U nucleotide and the last 3' position of the antisense region has neither an A nor U nucleotide;

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(d)   **after step (c)** selecting a candidate siRNA sequence from the set of candidate siRNA sequences of step (b) as an siRNA sequence for the target gene, if said candidate siRNA sequence satisfies said criterion; and

(e)   **after step (d)** generating an output comprising said siRNA sequence for the target gene, wherein said output is in a form that is readable by ~~at least one of a human or~~ computer.

62. (previously presented) The method according to claim 61, wherein the criterion is: within said duplex region the number of A and U nucleotides present in the first five nucleotide positions at the 5' terminus of the antisense region is higher than that present in the last five nucleotide positions at the 3' terminus of the antisense region.

63. (previously presented) The method according to claim 61, wherein the criterion is: within said duplex region the number of A and U nucleotides present in the first four positions at the 5' terminus of the antisense region is higher than that present in the last four positions at the 3' terminus of the antisense region.

64. (previously presented) The method according to claim 61, wherein the criterion is: within said duplex region the number of A and U nucleotides present in the first three positions at the 5' terminus of the antisense region is higher than that present in the last three positions at the 3' terminus of the antisense region.

65. (previously presented) The method according to claim 61, wherein the criterion is: within said duplex region the number of A and U nucleotides present in the first two positions at the 5' terminus of the antisense region is higher than that present in the last two positions at the 3' terminus of the antisense region.

66. (previously presented) The method according to claim 61, wherein the criterion is: within said duplex region the first 5' position of the antisense region has either an A or U nucleotide and the last 3' position of the antisense region had neither an A nor U nucleotide.

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67. (canceled)

68. (currently amended) A method for selecting an siRNA sequence for a target gene,
wherein said siRNA comprises an antisense sequence that is 19 – 30 nucleotide bases
in length and a sense sequence that is 19 – 30 nucleotide bases in length and said
antisense sequence and said sense sequence form a duplex region of 19-30 base
pairs, said method comprising the steps:

(a)   selecting a target gene;

(b)   identifying a set of candidate siRNA sequences, wherein the antisense sequence
        of each of said candidate siRNA sequences is at least 79% complementary to a
        region of the target gene;

(c)   applying to each of said candidate siRNA sequences, **a computer algorithm,
        wherein said computer algorithm comprises** a set of one or more criteria
        selected from the group consisting of a presence of U at position 1 of the
        antisense sequence, a presence of U at position 17 of the antisense sequence, a
        presence of A at position 10 of the antisense sequence, a presence of U at position
        6 of the antisense sequence, an absence of G at position 1 of the antisense
        sequence, an absence of C at position 7 of the antisense sequence, an absence of
        A at position 15 of the antisense sequence and an absence of U at position 9 of the
        antisense sequence, wherein said positions are defined in reference to the 5' end
        of the antisense sequence ~~within said duplex region~~;

(d)   **after step (c)** selecting a candidate siRNA sequence from the set of candidate
        siRNA sequences of step (b) as said siRNA sequence for the target gene, if said
        candidate siRNA sequence satisfies said set of one or more criteria; and

(e)   **after step (d)** generating an output comprising said siRNA sequence for the
        target gene, wherein said output is in a form that is readable by ~~at least one of a
        human or~~ computer.

69. (canceled)

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70. (previously presented) The method according to claim 68, wherein the set of one or more criteria includes the presence of U at position 1 of the antisense sequence.

71. (previously presented) The method according to claim 68, wherein the set of one or more criteria includes the presence of U at position 17 of the antisense sequence.

72. (previously presented) The method according to claim 68, wherein the set of one or more criteria includes the presence of A at position 10 of the antisense sequence.

73. (previously presented) The method according to claim 68, wherein the set of one or more criteria includes the presence of U at position 6 of the antisense sequence.

74. (previously presented) The method according to claim 68, wherein the set of one or more criteria includes the absence of G at position 1 of the antisense sequence.

75. (previously presented) The method according to claim 68, wherein the set of one or more criteria includes the absence of C at position 7 of the antisense sequence.

76. (previously presented) The method according to claim 68, wherein the set of one or more criteria includes the absence of A at position 15 of the antisense sequence.

77. (previously presented) The method according to claim 68, wherein the set of one or more criteria includes the absence of U at position 9 of the antisense sequence.

78. (previously presented) The method according to claim 1, wherein in (b) said antisense region is 100% complementary to said region of said target gene.

79. (previously presented) The method according to claim 43, wherein in (b) said antisense sequence is 100% complementary to said region of said target gene.

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80. (previously presented) The method according to claim 61, wherein in (b) said antisense region is 100% complementary to said region of said target gene.

81. (previously presented) The method according to claim 68, wherein in (b) said antisense sequence is 100% complementary to said region of said target gene.

82. (previously presented) The method according to claim 1, wherein said synthesizing comprises chemical synthesis.

83. (previously presented) The method according to claim 1, wherein said synthesizing comprises enzymatic synthesis.

84. (previously presented) The method according to claim 43, wherein said synthesizing comprises chemical synthesis.

85. (previously presented) The method according to claim 43, wherein said synthesizing comprises enzymatic synthesis.

86. (currently amended) A method for obtaining an siRNA molecule for a target gene, wherein said siRNA molecule comprises an antisense sequence that is 19 – 30 nucleotide bases in length and a sense sequence that is 19 – 30 nucleotide bases in length and said antisense sequence and said sense sequence form a duplex region of 19-30 base pairs, said method comprising the steps:

(a) selecting a target gene;

(b) identifying a set of candidate siRNA sequences, wherein the antisense sequence of each of said candidate siRNA sequences is at least 79% complementary to a region of the target gene;

(c) applying **to each of said candidate siRNA sequences a computer algorithm, wherein said computer algorithm comprises** a set of four or more criteria selected from the group consisting of: the presence of U at position 1 of the antisense

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sequence, the presence of U at position 17 of the antisense sequence, the presence of
A at position 10 of the antisense sequence, the presence of U at position 6 of the
antisense sequence, the absence of G at position 1 of the antisense sequence, the
absence of C at position 7 of the antisense sequence, the absence of A at position 15
of the antisense sequence, the absence of U at position 9 of the antisense sequence, a
GC content between about 30% and 52%, and at least 2 A or U bases at positions 1-5
of the antisense sequence wherein said positions are defined in reference to the 5' end
of the antisense sequence ~~within said duplex region~~;

(d) **after step (c)** selecting a candidate siRNA sequence from the set of candidate siRNA
sequences of step (b) as an siRNA sequence for the target gene, if said candidate
siRNA sequence satisfies said set of four or more criteria; and

(e) **after step (d)** synthesizing said siRNA molecule for said target gene, wherein said
siRNA molecule for said target gene comprises said siRNA sequence for the target
gene, whereby said siRNA molecule for said target gene is obtained.

87. (previously presented) The method according to claim 86, wherein in (c) said method
comprises applying a set of five or more criteria selected from the group consisting
of: the presence of U at position 1 of the antisense sequence, the presence of U at
position 17 of the antisense sequence, the presence of A at position 10 of the
antisense sequence, the presence of U at position 6 of the antisense sequence, the
absence of G at position 1 of the antisense sequence, the absence of C at position 7 of
the antisense sequence, the absence of A at position 15 of the antisense sequence, the
absence of U at position 9 of the antisense sequence, a GC content between about
30% and 52%, and at least 2 A or U bases at positions 1 - 5 of the antisense sequence,
and in (d) selecting said candidate siRNA sequence as said siRNA sequence for said
target gene if said candidate siRNA sequence satisfies said set of five or more
criteria.

88. (new) The method according to claim 1, wherein within the duplex the antisense
region and the sense region are 100 % complementary to each other.

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89. (new) The method according to claim 61, wherein within the duplex the antisense sequence and the sense sequence are 100 % complementary to each other.

90. (new) The method according to claim 88, wherein the antisense region and the sense region are each 19 bases in length.

91. (new) The method according to claim 89, wherein the antisense sequence and the sense sequence are each 19 bases in length.